Localized vasculitis of the gastrointestinal tract: a case series

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Abstract

Objective. To describe the clinical features and outcomes of patients with localized vasculitis of the gastrointestinal tract (LVGT).

Methods. Medical records of 608 patients diagnosed with vasculitis involving the intra-abdominal vasculature and/or abdominal viscera between January 1996 and December 2007 were reviewed. Only patients with histopathological confirmation or typical angiographic findings of vasculitis localized to the abdomen were included.

Results. We identified 18 cases with LVGT over the 12-year study period. The patients were predominantly Caucasian (89%) and female (67%) with a median age at diagnosis of 53.5 (range 17.4–83.3) years. Most of the patients presented with abdominal pain and 12 (66.6%) patients presented with an acute abdomen requiring surgical intervention. At diagnosis, the median ESR was 30.5 (range 4–77) mm/h. Autoantibody screening was generally unrevealing. Abdominal CT scan findings included: bowel wall thickening, bowel infarction and solid organ infarcts. In 14 patients, the diagnosis of vasculitis was established by abdominal angiography. Histological evidence of vasculitis was recorded in 5 (28%) patients, most commonly from gall bladder or small intestine specimens. Corticosteroid therapy was administered to 10 (56%) patients, 5 of whom also received other immunosuppressive agents. Median duration of follow-up was 10.5 (range 2–156) months. No evidence of vasculitis outside the abdomen was observed during follow-up. Seven (39%) patients died during the follow-up period. Survival of the patient cohort (compared with an age-matched US white population) was significantly reduced (P < 0.001).

Conclusion. LVGT is an uncommon form of vasculitis that can be associated with significant morbidity and mortality.

Key words: Vasculitis, Abdominal pain, Gastrointestinal tract, Mesenteric ischaemia, Gall bladder, Small intestine, Colon, Immunosuppressive therapy, Corticosteroids, Case series.

Introduction

The vasculitides are a group of conditions characterized by inflammation of blood vessel walls. The clinical spectrum is highly variable and vasculitis may be systemic or localized. Vasculitis involving the gastrointestinal (GI) tract often occurs as part of a systemic inflammatory process and is a well-recognized manifestation of small- and medium-sized vessel vasculitides. In particular, GI involvement frequently occurs in polyarteritis nodosa (PAN), ANCA-associated vasculitis (Wegener’s granulomatosis, Churg–Strauss syndrome and microscopic polyangiitis), Henoch–Schönlein purpura and Takayasu arteritis [1–4]. When present, GI complications adversely affect prognosis and are an indicator of disease severity [5]. Less commonly, GI involvement occurs in other forms of vasculitis, such as GCA [6, 7] and Behçet’s disease [8]. Furthermore, GI vasculitis may be present in patients with RA or CTDs, such as SLE [9].
Vasculitis of the GI tract may occur in isolation, and may represent a form of single-organ vasculitis (SOV). SOV has been reported to occur in the breast, aorta and in organs of the GI and genitourinary tracts. Focal SOV tends to have a good prognosis and excision of the vasculitic lesion can be curative, although SOV can also progress to a systemic illness [10]. Nevertheless, localized vasculitides of major organs such as the GI tract may have a significant impact on morbidity and premature mortality in the affected patients.

There are limited data in the literature regarding localized vasculitis of the GI tract (LVGT) and this entity is not well understood. The clinical features of LVGT have primarily been described in individual case reports and small case series [11–16]. The objective of this study is to describe the clinical features, radiographic characteristics and outcomes of a series of patients with LVGT seen at a tertiary care centre.

Patients and methods

Identification of patients

We used our institution’s medical record diagnostic linkage system to identify patients treated at the Mayo Clinic (Rochester, MN, USA and Jacksonville, FL, USA) from 1 January 1996 to 31 December 2007, who had a diagnosis of vasculitis involving the GI tract. We screened the text of the electronic medical records for a diagnosis of vasculitis in combination with key indexing terms. The following key words were used: mesenteric arteries, celiac artery, gastric artery, hepatic artery, splenic artery, oesophagus, stomach, small intestine, jejunum, ileum, appendix, colon, rectum, gall bladder, pancreas, liver and spleen. We reviewed records of all patients with findings of vasculitis involving the GI tract and excluded patients with other diagnoses (e.g. systemic necrotizing vasculitis, Takayasu arteritis, HSP, Behcet’s disease, RA and CTDs, etc.). This study was approved by the Mayo Clinic Institutional Review Board (IRB). Informed consent was not obtained for this study. The Mayo Clinic IRB reviewed and approved the study. The IRB approved waiver of specific informed consent in accordance with 45 Code of Federal Regulations 46.116 (d) as justified by the investigator, and waiver of health information portability and accountability Act (HIPAA) authorization in accordance with applicable HIPAA regulations.

Diagnostic criteria

The patients with LVGT were ascertained using the following criteria: (i) recent history or presence of acquired GI manifestations (included in Table 1); (ii) histopathological evidence of vasculitis in a GI specimen; or (iii) high-probability angiographic findings (smooth segmental narrowing, dilatation, occlusion or aneurysms affecting one or more GI arteries in the absence of vessel changes of atherosclerosis or vasculitis mimics such as fibromuscular dysplasia) with a report by the Mayo Clinic radiologist that specifically states that findings are consistent with a diagnosis of vasculitis.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients (n = 18), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>6 (33.3)/12 (66.7)</td>
</tr>
<tr>
<td>Age at diagnosis, years</td>
<td>53.5 (17.4–83.3)</td>
</tr>
<tr>
<td>Months from symptom onset to diagnosis</td>
<td>10 (0.5–45)</td>
</tr>
<tr>
<td>Follow-up period from the onset of symptoms, months</td>
<td>10.5 (2–156)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>17 (94.4)</td>
</tr>
<tr>
<td>Abdominal angina</td>
<td>8 (44.4)</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>12 (66.7)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>8 (44.4)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>13 (72.2)</td>
</tr>
<tr>
<td>Haematochezia or melaena</td>
<td>3 (16.7)</td>
</tr>
<tr>
<td>Gastroduodenal ulcers*</td>
<td>5/15 (33.3)</td>
</tr>
<tr>
<td>Gastroduodenal mucosal haemorrhage/active bleeding*</td>
<td>2/15 (13.4)</td>
</tr>
<tr>
<td>Colorectal ulcersb</td>
<td>3/12 (25)</td>
</tr>
<tr>
<td>Colorectal mucosal haemorrhage/active bleedingb</td>
<td>1/12 (8.3)</td>
</tr>
<tr>
<td>Acute abdomen</td>
<td>12 (66.6)</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>5 (27.7)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>Bowel perforation</td>
<td>1 (5.5)</td>
</tr>
<tr>
<td>Intestinal occlusion</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>GI ischaemia/infarction</td>
<td>7 (38.8)</td>
</tr>
<tr>
<td>Splenic infarction</td>
<td>4 (22.2)</td>
</tr>
<tr>
<td>Liver infarction</td>
<td>3 (16.6)</td>
</tr>
</tbody>
</table>

Continuous data are presented as median and range. Categorical data are presented as number and percentage of patients. *Upper endoscopy was performed in 15 patients; †colonoscopy was performed in 12 patients.

For cases where the diagnosis was not definitive, the investigators reviewed all available clinical, radiological and pathological data, and reached a consensus regarding the clinical diagnosis. Cases with angiograms showing a single abnormality in multiple arteries or multiple abnormalities in a single artery were reviewed again but generally excluded.

Data collection

A standard data collection form was completed on all confirmed cases containing information of the clinical symptoms at presentation and follow-up, comorbid medical conditions and all relevant laboratory investigations. Information from radiological images, pathological specimens and autopsy data were recorded, including CT and MRI, angiographic data and results of GI biopsy. In addition, information on treatment regimens, response to treatment, presence and number of relapses, follow-up functional status and cause of death, if appropriate, were documented as available from the chart. Response to therapy was determined according to documentation...
by the treating physician. Relapses were defined as an increase or progression of disease activity requiring an increase of therapy.

Statistical analysis
Descriptive statistics were used to summarize the data (percentages, means, etc.). The distribution of survival times following diagnosis date was estimated using Kaplan–Meier methods [17]. Expected survival was estimated by applying the age-, sex- and calendar year-specific mortality rates from the US White population to this cohort [18]. The one-sample log-rank test was used to test for a difference between observed and expected survival [19].

Results
Patients and diagnosis
Of the 608 patients diagnosed with vasculitis involving the intra-abdominal vasculature and/or abdominal viscera at the Mayo Clinic between 1996 and 2007, 18 patients fulfilled the diagnostic criteria for LVGT. The patients were predominantly Caucasian (89%) and female (67%) with a median age of 53.5 (range 17.4–83.3) years at diagnosis. The median time between symptom onset and diagnosis was 10 (range 0.5–45) months. The median duration of follow-up for all 18 patients was 10.5 (range 2–156) months. Comorbid conditions included: diabetes in two (11.1%) patients; hypertension in six (33.3%); coronary artery disease in one (5.6%); and hyperlipidaemia in four (22.2%). Seven (39%) patients were current or past smokers.

For 14 patients, the diagnosis was established by abdominal angiography. In one of them, vasculitis was confirmed at autopsy. For four patients, the diagnosis was established after histological examination of surgically removed GI tract specimens. Four patients had vasculitic involvement of medium-sized arteries and one of small vessels. In two patients, vasculitis involved the gall bladder; in one, gall bladder and pancreas; in one, appendix and small bowel; and in one, the large bowel. The histological patterns were acute necrotizing in four patients (Fig. 1) and granulomatous and necrotizing in another. No evidence of vasculitis outside the GI system was observed during the follow-up period.

Clinical findings
Table 1 lists the various GI clinical manifestations. Most patients had multiple manifestations. Abdominal pain was the most frequent finding, present in almost all patients. The pain was usually intense, and no preferential site could be identified. Other identified GI findings were abdominal angina, nausea or vomiting, diarrhoea, haematochezia or melaena. Weight loss was present in 13 (72.2%) patients [median 11 (range 2.5–24) kg] and fever in 4 (22.2%).

The clinical finding of an acute abdomen requiring exploratory abdominal surgery was present in 12 (66.6%) patients (Table 2). Of the 12 patients who developed acute abdomen, acute cholecystitis and/or gall bladder infarction were the most common diagnoses (five

![Fig. 1 Arteritis in the pancreas and gall bladder. Photomicrograph of the gall bladder (left panel) showing inflamed mucosa towards the top with transmural inflammation involving a submucosal muscular artery. The artery shows focal fibrinoid necrosis (lower right) as well as diffuse intimal fibroplasia [hematoxylin and eosin (H&E), x50]. Photomicrograph of the pancreas (right panel), removed as a Whipple specimen. Two muscular arteries are shown with segmental (middle) and complete (lower) necrotizing arteritis with fibrinoid degeneration of the arterial wall. Dense perivascular lymphoplasmacytic inflammation is seen. The pancreatic parenchyma toward the top is relatively well preserved (H&E, x100).](image-url)
<table>
<thead>
<tr>
<th>Patient/age/sex</th>
<th>Angiography</th>
<th>Surgery/histopathology</th>
<th>Treatment</th>
<th>Follow-up period*</th>
<th>Status at last follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/84/F</td>
<td>Positive</td>
<td>Not done</td>
<td>Not treated</td>
<td>2 months</td>
<td>Death (unknown cause)</td>
</tr>
<tr>
<td>2/71/F</td>
<td>Positive</td>
<td>Not done</td>
<td>Not treated</td>
<td>7 months</td>
<td>Death (unknown cause)</td>
</tr>
<tr>
<td>3/19/M</td>
<td>Negative</td>
<td>Cholecystectomy; gall bladder necrotizing vasculitis</td>
<td>Not treated</td>
<td>33 months</td>
<td>In remission</td>
</tr>
<tr>
<td>4/48/F</td>
<td>Not done</td>
<td>Pancreatectomy and cholecystectomy; necrotizing vasculitis in gall bladder walls and pancreas</td>
<td>Oral pred (initial dosage, 60 mg/day) for 9 months, Oral CYC (100 mg/day) for 9 months</td>
<td>13 years</td>
<td>In remission, off therapy</td>
</tr>
<tr>
<td>5/65/M</td>
<td>Positive</td>
<td>Cholecystectomy; acute cholecystitis with extensive necrosis</td>
<td>i.v. MP (1 g/day) for 3 days, then oral pred (initial dosage: 60 mg/day) for 11.5 months, i.v. CYC (1.3 g/month) for 5 months</td>
<td>13.5 months</td>
<td>Death from multiple hepatic abscesses, on therapy (oral pred 12.5 mg/day), improved follow-up angiogram</td>
</tr>
<tr>
<td>6/61/F</td>
<td>Positive</td>
<td>Two jejunum surgical resections; ischaemic necrotic jejunum</td>
<td>Oral pred (initial dosage, 40 mg/day) for 1 month</td>
<td>7 months</td>
<td>In remission, on therapy (pred 40 mg/day)</td>
</tr>
<tr>
<td>7/37/F</td>
<td>Positive</td>
<td>Bowel obstruction requiring two resections of the small intestine; patchy ulcerations and chronic enteritis; appendectomy: normal appendix</td>
<td>Oral pred (initial dosage, 30 mg/day) for 7 months</td>
<td>16 months</td>
<td>In remission, off therapy</td>
</tr>
<tr>
<td>8/62/F</td>
<td>Positive</td>
<td>Colonoscopy: ischaemic colitis Resections of jejunum and oesophagus: chronic inflammation and subepithelial fibrosis</td>
<td>Not treated</td>
<td>48 months</td>
<td>Death (unknown cause)</td>
</tr>
<tr>
<td>9/62/M</td>
<td>Positive</td>
<td>Upper endoscopy: ischaemic duodenitis and jejunitis Colonoscopy: ischaemic colitis Autopsy: small and large bowel ischaemia, small–vessel necrotizing vasculitis, focal lymphocytic infiltration</td>
<td>Not treated</td>
<td>2 months</td>
<td>Death: Gl haemorrhage, small and large bowel ischaemia</td>
</tr>
<tr>
<td>10/27/F</td>
<td>Positive</td>
<td>Exploratory laparotomy: small and large bowel ischaemia, SMA by-passes</td>
<td>Not treated</td>
<td>37 months</td>
<td>Active vasculitis (relapse: ischaemic bowel)</td>
</tr>
<tr>
<td>11/47/F</td>
<td>Positive</td>
<td>Cholecystectomy; cholecystitis</td>
<td>Oral pred (initial dosage, 50 mg/day) for 1 month</td>
<td>9 months</td>
<td>Death from hepatic infarcts and ischaemic gastroparesis, on therapy (pred 50 mg/day)</td>
</tr>
<tr>
<td>12/45/M</td>
<td>Positive</td>
<td>Exploratory laparotomy for bowel obstruction: negative Colonoscopy: ischaemic colitis Not done</td>
<td>Oral pred (initial dosage, 100 mg/day) for 2 months</td>
<td>6 months</td>
<td>Death from abdominal perforation and peritonitis, on therapy (pred 50 mg/day)</td>
</tr>
<tr>
<td>13/42/M</td>
<td>Positive</td>
<td></td>
<td>i.v. MP (1 g/day) for 3 days, then oral pred (initial dosage 60 mg/day) for 36 months, Oral AZA (150 mg/day) for 19 months MTX (10 mg/week) for 9 months</td>
<td>36 months</td>
<td>In remission, on therapy (pred 1 mg/day, MTX 10 mg/week)</td>
</tr>
<tr>
<td>14/59/M</td>
<td>Positive</td>
<td>Right common iliac to SMA by-pass and SMA endarterectomy Resection of ischaemic small intestine Coil embolizations of SMA jejunal branches Colonoscopy: ischaemic colitis</td>
<td>i.v. MP (1 g/day) for 5 days, then oral pred (initial dosage, 60 mg/day) for 15 months, i.v. CYC (1.5 g/month) for 11 months and oral CYC (200 mg/day) for 1 month, Oral AZA (60 mg/day) for 3 months</td>
<td>19 months</td>
<td>In remission, on therapy (pred 9 mg/day, AZA 50 mg/day)</td>
</tr>
</tbody>
</table>

(continued)
patients; Patients 3–5, 11 and 18), followed by bowel infarction (three patients small bowel, one small and large bowel; Patients 6, 10, 14 and 16). Two patients underwent exploratory laparotomy for bowel obstruction (Patients 7 and 12). Patient 12 died 3 months later of bowel perforation and peritonitis. The last patient (Patient 8) had progressively worsening abdominal pain, nausea and vomiting with a weight loss of 16 kg in the year before evaluation at the Mayo Clinic.

Patient 8 had undergone a total gastrectomy for massive gastric ulcerations and partial small bowel resection for ischaemia performed 14 years previously, and subsequently multiple unsuccessful dilatations for chronic stricture at the oesophagojejunostomy anastomosis. A colonoscopy revealed the presence of ischaemic colitis and abdominal angiogram demonstrated the presence of multiple stenoses and dilatations in inferior mesenteric artery branches suggestive of vasculitis. Resection of small bowel, jejunum and oesophagus was performed and the histological examination showed only chronic inflammation and subepithelial fibrosis.

GI bleeding was observed in three patients (Patients 1, 9 and 14) and was the main presenting manifestation in Patient 1, who did not present with abdominal pain. In Patient 1, upper endoscopy revealed multiple superficial gastric ulcerations without evidence of bleeding. In Patient 9, upper endoscopy revealed bleeding duodenal ulcers and ischaemic changes in distal duodenum and proximal jejunum, whereas in Patient 14, duodenal ulcers and jejunal ulceration with a clot was noted. In Patient 1, tagged red blood cell study showed bleeding in the distal ileum. There was also evidence of ischaemic colitis at colonoscopy in Patients 9 and 14.

In total, upper endoscopy was performed in 14 patients, revealing ulcers in 5 patients, bleeding in 2 and ischaemic changes in 1. Twelve patients underwent colonoscopy with evidence of ischaemic colitis in four patients (Patients 8, 9, 12 and 14). There was evidence of tarry stool in the colon in Patient 1; however, the bleeding site was not identified by this examination.

**Imaging**

Fifteen patients underwent abdominal angiography and in 14 there were changes characteristic of vasculitis (Table 2 and Fig. 2). Conventional angiography was performed in 14 patients, magnetic resonance angiography (MRA) in 5 and CT angiography in 6.

All patients had multiple lesions of the multiple GI arteries. The distribution of arterial involvement is shown in detail in Table 3. Stenosis was the most frequent lesion, present in 13 (86.7%) patients, followed by dilatation in 8 (53.3%), aneurysm in 5 (33.3%), obstruction in 4 (26.7%) and wall thickening in 2 (13.3%). The most commonly involved blood vessel was the superior mesenteric artery (73.3%), followed by celiac artery (60%), hepatic artery (53.3%), inferior mesenteric artery (46.7%), splenic artery (40%) and gastric artery (6.7%). One patient had only abdominal MRA, which did not reveal vasculitic lesions (Patient 3).
Three patients also underwent MRA and two others CT angiography of thoracic aorta and its branches. There was no evidence of vasculitic involvement in these vessels in these patients. Abdominal CT was performed in 12 patients. Spleen infarcts were present in three patients, liver infarcts in two, bowel infarction in two, small intestine and/or large intestine wall thickening in three.

**Table 3** GI vascular involvement in 15 patients undergoing angiography

<table>
<thead>
<tr>
<th>Artery</th>
<th>Any lesion</th>
<th>Stenosis</th>
<th>Occlusion</th>
<th>Dilatation</th>
<th>Aneurysm</th>
<th>Wall thickening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior mesenteric</td>
<td>11 (73.3)</td>
<td>10 (66.7)</td>
<td>2 (13.3)</td>
<td>6 (40)</td>
<td>3 (20)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Celiac</td>
<td>9 (60.0)</td>
<td>7 (46.7)</td>
<td>2 (13.3)</td>
<td>2 (13.3)</td>
<td>3 (20)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Hepatic</td>
<td>8 (53.3)</td>
<td>5 (33.3)</td>
<td>3 (20.0)</td>
<td>3 (20.0)</td>
<td>1 (6.7)</td>
<td>0</td>
</tr>
<tr>
<td>Inferior mesenteric</td>
<td>7 (46.7)</td>
<td>5 (33.3)</td>
<td>1 (6.7)</td>
<td>4 (26.7)</td>
<td>0</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Splenic</td>
<td>6 (40.0)</td>
<td>4 (26.7)</td>
<td>3 (20.0)</td>
<td>0</td>
<td>2 (13.3)</td>
<td>0</td>
</tr>
<tr>
<td>Gastric</td>
<td>1 (6.7)</td>
<td>1 (6.7)</td>
<td>0</td>
<td>0</td>
<td>1 (6.7)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Conventional angiography was only performed in six patients, MRA only in one, conventional angiography and MRA in two, conventional angiography and CT assisted angiography in four, and all three angiographic techniques were utilized in two patients.*

**Fig. 2** CT of the abdomen (axial view) demonstrates a thick-walled aneurysm of the celiac artery (A). MR of the abdomen demonstrates long segment high-grade stenoses of the proximal celiac and superior mesenteric artery (B). CT angiogram of the abdomen demonstrates diffuse wall thickening of the proximal and mid superior mesenteric artery resulting in diffuse luminal stenosis (C, magnified inset).

**Laboratory findings**

ESR was measured in all 18 patients at diagnosis. The ESR was increased (>30 mm/h) in nine (50%) patients. The median ESR was 30.5 (range 4–77) mm/h. Serum tests results were negative for anti-neutrophil cytoplasmic antibodies (0/17), ANA (0/16), RF (0/16), cryoglobulins (0/
16), anti-phospholipid antibodies (0/9), hepatitis B virus serology (0/15) and HIV serology (0/4) in all patients in whom these were measured. Complement levels were tested in eight patients and they were normal. Hepatitis virus C serology was tested in 15 patients and was positive in 1 patient 6 years after the onset of vasculitis symptoms. Hepatic biopsy was normal. Extensive thrombophilic screening was performed in eight patients, without abnormal findings.

**Therapy and outcome**

Of the 18 patients with LVGT identified in this case series, 10 patients were treated medically and 8 were not. All the medically treated patients received oral prednisone. The median starting dosage of oral prednisone therapy was 60 (range 30–100) mg/day. In three patients oral prednisone treatment was preceded by methylprednisolone pulse therapy (1 g/day for 3 days in two patients and 1 g/day for 5 days in one) (Patients 5, 13 and 14). The median duration of oral prednisone therapy was 7.5 (range 1–36) months.

The details of treatment and the status of patients at last follow-up for all 18 patients are shown in Table 2. Five patients initially were treated with prednisone alone, and five were treated with corticosteroids and multiple immunosuppressive agents. Three patients received daily oral cyclophosphamide (100 mg/day for 9 months and 2 months, and 200 mg/day for 1 month) (Patients 4, 14 and 17). Patients 5 and 14 received monthly intravenous cyclophosphamide pulse therapy (1.3 g/month for 5 months and 1.5 g/month for 11 months). Two patients also received AZA (150 and 50 mg/day for 19 and 3 months, respectively; Patients 13 and 14) and one patient received MTX (10 mg/week for 9 months; Patient 13).

Eight patients responded to therapy. Response was also noted in five patients who had relapses (Patients 5, 13, 14, 16 and 17). Patients 11 and 12 had a catastrophic course and the inflammatory process was never controlled by the therapy. At the last follow-up, of the 10 patients receiving medical treatment, 2 were in remission without therapy (Patients 4 and 7), 5 were in remission on treatment (Patients 6, 13, 14, 16 and 17) and 3 patients died (Patients 5, 11 and 12). Patients 11 and 12 died 1 and 2 months after the diagnosis, respectively, whereas on therapy with prednisone 50 mg/day of causes directly related to vasculitis: one of hepatic infarction and ischaemic gastroparesis, the second of abdominal perforation and peritonitis. Patient 5 died of multiple hepatic abscesses 11.5 months after the diagnosis. He was on therapy with prednisone 12.5 mg/day; a follow-up angiogram performed 2 weeks prior to death showed improvement.

At the last follow-up, of the eight untreated patients, three were in remission (follow-up duration: 2.5, 9 and 33 months; Patients 3, 15 and 18), one had a relapse of the vasculitis (ischaemic bowel) that required surgery 37 months after the onset of symptoms (Patient 10) and four had died (Patients 1, 2, 8 and 9). In Patients 3 and 18 the vasculitis process was completely resolved without recurrence following surgical intervention (cholecystectomy).

Patient 15 had a spontaneous complete resolution of her GI manifestations. Three died of unknown causes (0.5, 4.5 and 34 months after the diagnosis) and one of GI haemorrhage related to bowel ischaemia 7 days after the initial diagnosis of vasculitis. In this last patient the autopsy showed evidence of active large bowel vasculitis.

Twelve (66.6%) patients underwent surgical intervention. Cholecystectomy was performed in four patients (Patients 3, 5, 11 and 18); small bowel resection in two (Patients 6 and 8); appendectomy and small bowel resection in two (Patients 7 and 16); cholecystectomy and pancreaticoduodenectomy in one (Patient 4); and small bowel resection, superior mesenteric artery bypass, endarterectomy and arterial embolization in one (Patient 14). Two other patients had exploratory laparotomy for ischaemic bowel (Patient 10) and bowel obstruction (Patient 12). In Patient 10 superior mesenteric artery bypass was performed, whereas no abnormalities were observed in Patient 12.

Four of the twelve patients receiving surgical intervention received no drug treatment (Patients 3, 8, 10 and 18). Two of them had gall bladder vasculitis (Patients 3 and 18) and remained in complete remission during the follow-up period.

Figure 3 shows an estimated age- and sex-matched survival curve of patients with LVGT and the expected survival curve of an age-matched US White population. Survival of patient cohort was significantly reduced (P < 0.001).

**Discussion**

In the current study we have identified and described 18 patients with LVGT, which, to our knowledge, is the largest series reported to date. We specifically excluded patients with any evidence of vasculitis outside the GI tract, either at initial presentation or during the follow-up period, ensuring a relatively homogenous sample.

The clinical features of LVGT in our series appear to be similar to those described in case reports of LVGT in the
GI vasculitis

literature [11–13, 15, 20]. GI manifestations of systemic vasculitis also present with abdominal pain, nausea/vomiting, diarrhoea or symptoms of GI bleeding and therefore may be indistinguishable from clinical features of LVGT [9]. Two-thirds of patients in the current series presented with an acute abdomen requiring surgical intervention, whereas only about one-third of patients had a surgical abdomen in a series of patients with systemic vasculitis and GI involvement [9]. In patients with PAN and GI involvement, more than half develop an acute surgical abdomen and this portends a worse prognosis [21].

The laboratory features found in patients with LVGT are non-specific. Inflammatory markers may be elevated, although half of the patients in the current series had an ESR <30 mm/h. Autoantibody profiles were negative in all patients. Conversely, patients with systemic vasculitis or CTD with GI involvement frequently have positive autoantibodies including ANA and ANCA serologies [9, 22].

Vasculitis of the GI tract may result in varied imaging findings. Abdominal CT findings could include non-specific organomegaly, focal mass lesions [11, 23, 24], parenchymal infarctions affecting the kidneys or spleen [9] and intestinal wall thickening [9, 12, 13]. However, non-invasive diagnosis of GI vasculitis is usually made by angiography. In the current series, 14 patients had changes characteristic of vasculitis including vascular stenoses, dilatation, aneurysms, obstruction and wall thickening. These angiographic features have been well characterized in patients with systemic medium-vessel vasculitis, mainly PAN [25, 26]. Most cases were diagnosed by conventional catheter-based angiography. More recently, CT or MR angiography is being increasingly utilized for the evaluation of medium- and large-vessel vasculitis. The latter techniques have the added advantage of visualizing the vessel wall for thickening/oedema, which could be suggestive of vasculitis [27].

At times, it may be difficult to distinguish fibromuscular dysplasia from vasculitis. Their angiographic appearance may be similar, in particular in patients with intimal fibroplasia involving multiple vessels [28]. Changes in acute-phase reactants (fibromuscular dysplasia is a non-inflammatory process) and evidence of wall thickening/oedema at CT or MR angiography are useful to differentiate vasculitis from fibromuscular dysplasia. We included only patients with conventional angiograms clearly consistent with a diagnosis of vasculitis. Furthermore, cases with angiograms showing a single abnormality in multiple arteries or multiple abnormalities in a single artery were reviewed again but generally excluded.

Burke et al. [22] reported a large series of patients with GI vasculitis, including the clinical and pathological findings of 83 patients presenting with vasculitis of the GI tract identified from the records of the Armed Forces Institute of Pathology between 1970 and 1992. All the cases had pathological evidence of vasculitis defined as transmural inflammation of the wall of at least two vessels without surrounding soft tissue inflammation or necrosis. Cases with known systemic vasculitic involvement at the time of surgery were excluded from the study. However, the authors included patients with a diagnosis of RA or SLE, introducing a bias in patient selection because these two conditions can be associated with GI vasculitis. A further limitation of the study is that when followed over time, 6 of 23 patients with “isolated” polyarteritis of GI tract subsequently developed systemic vasculitis. Therefore, an adequate follow-up period is crucial to differentiate patients with LVGT from those who go on to develop a systemic vasculitis. The series also includes patients with Churg–Strauss granulomatosis, patients with Buerger’s disease as well as others with phlebitis of the GI vessels, suggesting that this was a heterogeneous group of cases [22].

In the current series, two patients were diagnosed with isolated vasculitis of the gall bladder. Gall bladder vasculitis may be a manifestation of systemic vasculitis, particularly PAN [9, 29] and ANCA-associated vasculitis [30]. However, it may also occur as a form of SOV, often discovered incidentally following cholecystectomy for cholelithiasis or cholecystitis [22, 31–34]. Isolated vasculitis of the gall bladder is typically associated with a favourable prognosis and surgical resection is often curative [10]. Both patients with isolated vasculitis of the gall bladder in the current series did well with surgical resection alone. Neither patient required immunosuppression and there was no evidence of systemic vasculitis, although one patient had limited follow-up. Vasculitis involving the pancreas is rare, even in the context of systemic vasculitic disorders [9]. Patients with localized vasculitis of the pancreas typically present with abdominal pain and evidence of a pancreatic mass on ultrasound or CT scan of the abdomen [11, 22–24]. Most cases of isolated vasculitis of the pancreas reported in the literature were managed surgically and had no evidence of systemic vasculitis during follow-up [11, 22, 34]. In a few cases, the patients were treated with corticosteroids and cyclophosphamide [23, 24]. The patient with vasculitis of the pancreas in our series also had histological evidence of vasculitis involving the gall bladder. She received immunosuppressive therapy following surgery and remained recurrence free after 13 years of follow-up.

PAN and ANCA-associated vasculitis can also involve the appendix [9]. On the other hand, SOV of the appendix can be an incidental finding in up to 1% of surgically excised appendices and usually does not require medical treatment [22, 35, 36]. In the current series, we did not identify patients with SOV of the appendix. However, one patient was treated with corticosteroids for extensive vasculitis of the small bowel and mesentery with involvement of the appendix. Localized vasculitis in the small and large intestine (diagnosed histologically) has been described in several reports [12, 15, 20, 22, 37–39]. While some patients with isolated vasculitis of the small or large intestine did well with surgical resection alone [20, 37], others required immunosuppressive therapy [12, 38]. In the current series, two patients had histologically confirmed vasculitis involving the bowel wall. One patient (Patient 9) died of multiorgan failure and the
diagnosis was confirmed at autopsy, whereas the other patient (Patient 16) received corticosteroid therapy postoperatively and did well.

Overall, the outcome of LVGT is very variable. In general, patients with SOV involving the gall bladder, pancreas and appendix are cured by surgical intervention only and the prognosis is excellent. Patients with involvement of the intestinal wall have a more variable outcome depending on disease extent and immunosuppressive treatment. Most patients in the current series had medium-vessel vasculitis detected on angiography and, of these, only 50% were alive at the end of the study (median follow-up 10.5 months). The overall mean survival of 6.7 months in our study is largely driven by this group of patients. Pagnoux et al. [9] reported a 5-year survival rate of 76% (95% CI 65, 87) in a group of 62 patients with systemic vasculitis and GI involvement. The 5-year survival rate for patients with surgical abdomen was 56% (95% CI 35, 77) and the survival rate was 82% (95% CI 70, 94) for those without [9]. Some patients with LVGT may have a worse prognosis because of lack of serological markers leading to delay in diagnosis and, possibly, delayed treatment.

Our study has several limitations. All patients in this series were evaluated at a tertiary care institution and, therefore, the study is susceptible to referral bias. This series may not be representative of patients who have LVGT that is cured surgically in community practices. However, population-based studies of patients with LVGT would not be feasible due to the rarity of the condition. Therefore, one cannot confidently establish the incidence or prevalence of this condition. There is also a possible bias towards inclusion of patients with LVGT because disease extent may not have been systematically assessed in all cases. However, most of our reported cases were evaluated by a rheumatologist during the course of their illness. The current study was retrospective and therefore only reflects information already present in the medical record. The small sample size in this study precludes analyses to correlate treatment and/or outcome with particular disease subsets.

Histological documentation of LVGT was available only in five cases in this series. In the remainder of the cases, we used typical features of vasculitis recorded on arterial imaging to establish the diagnosis. One of the strengths of our case series is that it includes both patients diagnosed with LVGT by histopathology and those diagnosed by radiographic studies. Previously reported cases of LVGT have generally been defined based on the histological diagnosis of vasculitis. However, patients with angiographically defined LVGT must also be considered in order to recognize the complete clinical spectrum of this condition.

This largest series of LVGT reported to date reveals this uncommon form of vasculitis to be associated with significant morbidity and mortality. Laboratory tests are non-specific and the diagnosis is usually based on characteristic radiographic imaging studies and/or histopathological examination of surgical specimens. Optimal treatment remains to be defined.

Rheumatology key messages

- Patients with LVGT typically present with abdominal pain; the diagnosis requires radiographic imaging studies or histopathological examination of surgical specimens.
- Although uncommon, LVGT can be associated with significant morbidity and mortality.

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References